

[0068] In a preferred embodiment, the magnetic beads are non-uniform in size. Generally, any shape beads may be used, that is, any shape having an angle or curvature will form gradients. Heterogeneous materials might be used to accomplish separations of targets with varying magnetic susceptibilities. While smaller magnetic beads produce higher magnetic force density, as explained above, larger beads produce a magnetic field gradient that reaches further from their surface. Generally, this is attributable to the higher radius of curvature of the smaller beads. Due to this smaller radius of curvature, smaller beads have stronger gradients at their surface than larger beads. The smaller beads also generally have gradients that fall off more rapidly with distance. Further, the magnetic flux at a distance will generally be less for a smaller bead. A mixture of small and big magnetic beads thus will capture both weakly magnetized materials (i.e., by smaller beads) and strongly magnetized materials that are far from the beads (i.e., by bigger beads). Combinations of magnetic beads with various sizes will allow one to create a desired gradient within the channel and create a high target capture efficiency. The present invention is in stark contrast to conventional magnetic separation techniques, which have emphasized on a uniform magnetic field inside the chamber/channel. In fact, in some applications of the present invention, uniform bead size is not necessarily a requirement and may even be detrimental to some applications. Preferred bead sizes generally range from about 10 μm -1 mm, although in some embodiments larger or smaller beads may be used.

[0069] In a preferred embodiment, the magnetic microchannel comprises at least one section comprising magnetic beads. This can be accomplished in three general ways: the magnetic beads may be embedded in one or more sections of the wall of the microchannel; the magnetic beads may be coated on one or more sections of the walls of the microchannel; or the magnetic beads may be packed into one or more sections of the microchannel.

[0070] By "walls" herein is meant the inner surface of the microchannel, or the substrate immediately surrounding the outer surface of the microchannel. By "section" herein is meant either a discrete area on the walls of the magnetic microchannel, or a portion of the inner channel chamber having the same diameter but a shorter length than the entire channel. Preferably, the wall or chamber along the entire length of the magnetic microchannel comprise magnetic beads for the highest efficiency. However, it is also possible that only one or more sections of the magnetic microchannel comprise magnetic beads.

[0071] The sections on the wall of the channel can have various sizes, shapes, and configurations. For example, one or more sections on the wall can be bands that surround the magnetic microchannel. Alternatively, the sections can be restricted to the lateral sides of the channel. The various sections can either be arranged in a variety of configurations, either randomly or in an ordered manner.

[0072] In a preferred embodiment, the magnetic beads are embedded in the walls of the magnetic microchannel (i.e., an "embedded channel"). More specifically, the magnetic beads are present in the substrate surrounding the outer surface of the microchannel. These beads can be in a single layer, or more preferably in multiple layers. The maximum number of

the layers depends on the thickness of the substrate, the size of the beads, and/or the configuration of channels/components on the substrate.

[0073] While the magnetic beads in the embedded channel will generate a local high gradient magnetic field within the microchannel, they are present outside of the microchannel, thus guaranteeing a uniform flow within the channel and a consistent processing result. Because the sample flowing through the channel will not be in direct contact with the magnetic beads, many problems can be avoided. For example, avoiding direct contact between the magnetic beads with the samples eliminates the problem of non-specific binding or trapping of the sample in the channel, making it easier to wash and recover the sample. Damages to sensitive materials in the sample or to the magnetic beads due to direct contact between the sample and the magnetic beads can also be avoided. Furthermore, the channels can be easily washed after each experiment, making it possible to reuse the inventive device.

[0074] In a preferred embodiment, the magnetic beads are coated on the inner surface of the microchannel (i.e., a coated channel). Because the volume of the inner channel chamber will have to accommodate the magnetic beads, the depth of the microchannel will generally be deeper than the embedded channel. On the other hand, because the dimension of the microchannel is restricted by the overall design of the device, the number of the layers of beads in the coating could be limited. It is preferred, though not necessary, that the inner surface of the channel that is not coated with the magnetic beads is coated with a coating of the same thickness, so that the inner space of the channel will be uniform throughout the channel.

[0075] Like the embedded channel, the coated channel also allows a uniform flow within the channel and a consistent processing result. Furthermore, coated channels are easier to fabricate, and has less requirement for the material that makes up the channel, as described below.

[0076] In a preferred embodiment, the magnetic beads are packed into a microchannel (e.g., a "filled-channel"). The general design of a macroscale of such apparatus is taught by U.S. Pat. Nos. 5,705,059 and 5,711,871, incorporated herein as reference. Generally, the channel dimension is chosen according to the bead size in these embodiments. The design above requires uniform beads which would be in the range of about 10 μm -1 mm for a monolayer of beads. Devices could be designed with several layers, however, and the channel height may then be a multiple of this-generally, up to several millimeters for 1 mm beads.

[0077] In a preferred embodiment, the magnetic beads packed in the microchannel are substantially symmetrically spherical in shape. Such spheres can assume a lattice configuration wherein the gaps between the spheres form regular channels or pores in the matrix. The lattice configuration is a patterned framework of spheres that form channels of regular size between adjacent spheres and throughout the matrix. Upon the application of an external magnetic field to the magnetic microchannel, magnetic field gradients are created in the gaps between the spheres.

[0078] In a preferred embodiment, the sizes of the magnetic beads packed in the magnetic microchannel are relatively homogeneous, usually varying not more than about